INTERVENTIONAL CARDIOLOGY AND SURGERY

Treatment of bifurcation lesions with two stents: one year angiographic and clinical follow up of crush versus T stenting

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Accepted 8 June 2005 Published Online First 17 June 2005 **Objectives:** To compare long term outcomes of the crush versus the T technique in bifurcation lesions. **Design:** 182 consecutive patients were identified who underwent percutaneous coronary interventions for bifurcation lesions with drug eluting stents between April 2002 and January 2004. Two techniques were used according to the operator's discretion: crush (group C, n = 121) or T (group T, n = 61). **Results:** In-hospital outcome differed significantly between the two groups. Angiographic follow up was available for 142 (78%) patients. Groups C and T did not differ significantly regarding late loss (0.42 (0.39) mm v 0.34 (0.35) mm, p = 0.52) and rate of restenosis (16.2% v 13.0%, p = 0.80) in both the main and the side branch without final kissing balloon post-dilatation. However, when final kissing balloon post-dilatation was performed, group C had significantly lower late lumen loss (0.23 (0.21) mm v 0.37 (0.33) mm, p = 0.02) and restenosis rate (8.6% v 26.5%, p = 0.04) in the side branch. At one year's clinical follow up, group C compared with group T had lower rates of target lesion revascularisation (14.0% v 31.1%, p = 0.01) and target vessel revascularisation (16.5% v 32.8%, p = 0.02).

Conclusions: In non-selected bifurcation lesions treated with drug eluting stents, the restenosis rate remains relatively high in the side branch. Compared with the T stenting technique, crush stenting with kissing balloon post-dilatation is associated with a reduced rate of restenosis in the side branch.

ecently, the randomised sirolimus eluting stent (SES) (Cypher; Cordis/Johnson & Johnson, Warren, New Jersey, USA) bifurcation study showed promising results compared with historical data on bare metal stents for the treatment of bifurcations. However, restenosis of the side branch after SES implantation remains a problem, possibly because of incomplete coverage of the ostium.¹ To overcome this limitation, the crush technique has been proposed as a method to implant two drug eluting stents (DES) with the intent to provide optimal lesion coverage and hence reduce the rate of restenosis at the side branch.2 Despite this theoretical advantage, the long term outcomes of this technique remain unclear. The purpose of this study was to evaluate the long term results with the crush technique and to compare them with results obtained with the T technique to gain insight into the appropriate technique to treat bifurcation lesions with DES when both the main and side branches require a stent.

METHODS

Study population

Demographic and procedural data regarding all patients undergoing angioplasty at EMO Centro Cuore Columbus and San Raffaele Hospitals were prospectively entered onto a dedicated database. All consecutive patients treated with DES, either SES or paclitaxel eluting stent (PES) (Taxus, Boston Scientific, Natick, Massachusetts, USA), in bifurcation lesions requiring two stents between April 2002 and January 2004 were identified. Patients were excluded if any of the following was present: acute myocardial infarction (AMI) in the 24 hours preceding the index procedure; bifurcation lesions in the left main vessel; or treatment with V stenting or culotte stenting.

Patients were divided into two groups based on the stenting techniques used: crush stenting (group C) and T or

modified T stenting (group T). The selection of a specific strategy was left to the operator's decision. The T and modified T stenting technique predated the usage of crush stenting. The decision to use two stents was based on the presence of at least one of the following criteria: the side branch had a diameter of at least 2.25 mm (visual estimate) and was significantly narrowed at the ostium or within a few millimetres of it; the angle between the two branches was < 45°; and significant plaque shift was expected.

Procedures and postinterventional medications

The crush technique has been previously described.2 In our initial experience, final kissing balloon inflation was not performed routinely when no residual stenosis was observed at the ostium of the side branch. Since January 2003, kissing inflation became our standard practice. In patients who underwent kissing balloon post-dilatation, the wire was always recrossed into the side branch followed by high pressure (12-14 atm) balloon inflation before kissing balloon post-dilatation was applied. A floppy wire or an intermediate wire, occasionally a hydrophilic or partially hydrophilic wire (Pilot 150, Guidant, Temecula, California, USA; Asahi Prowater, Asahi Intecc, Nagoya, Japan), was chosen to recross into the side branch. In four patients, despite wire advancement, a balloon could not be deployed and a fixed wire system (ACE, Boston Scientific/Scimed, Maple Grove, Minnesota, USA) was used with success.

All patients were pre-treated with aspirin and either ticlopidine or clopidogrel. A 300 mg loading dose of clopidogrel was administered before the index procedure if

Abbreviations: AMI, acute myocardial infarction; CI, confidence interval; CK, creatine kinase; DES, drug eluting stents; PES, paclitaxel eluting stent; SES, sirolimus eluting stent; TLR, target lesion revascularisation; TVR, target vessel revascularisation

patients were not pre-treated. During the procedure, patients received intravenous unfractionated heparin (100 IU/kg) to maintain activated clotting time between 250–300 seconds. Administration of glycoprotein IIb/IIIa inhibitors was left to the operator's discretion. Post-procedural creatine kinase (CK) was routinely measured in all patients after the index procedure. Measurements were repeated in case of a rise in CK over the upper normal limit. All patients were maintained with aspirin, and clopidogrel or ticlopidine was administered for at least six months after DES implantation.

Clinical definitions and follow up

Clinical follow up was conducted by telephone contact or office visit throughout the entire follow up period. Angiographic follow up was scheduled for between six and eight months after the procedure unless clinically indicated earlier.

Major adverse cardiac events were defined as cardiac death, AMI, and target vessel revascularisation (TVR), either percutaneous or surgical. All deaths were regarded as cardiac unless otherwise documented. A non-Q wave AMI was defined as a CK concentration rise > 2 times the upper limit of the normal with an increased CK-MB concentration in the absence of pathological Q waves. Target lesion revascularisation (TLR) was defined as a repeat revascularisation with a stenosis $\ge 50\%$ in the target lesion in either the main branch or the side branch. TVR was defined as any repeat revascularisation within the treated vessel.

Stent thrombosis was defined as an acute coronary syndrome with angiographic documentation of either vessel occlusion or thrombus within or beside a previously successfully stented vessel or, in the absence of angiographic confirmation, either AMI in the distribution of the treated vessel or death not clearly attributable to other causes.^{3–5} According to the timing of the events stent thrombosis were categorised as intraprocedural,⁶ subacute (after the end of the procedure to 30 days), or late (> 30 days).

Quantitative coronary angiographic analysis

Cineangiograms were analysed with a validated edge detection system (CMS, version 5.2; MEDIS, Leiden, the Netherlands) at baseline, after the procedure, and at follow up. The type of bifurcation lesions was categorised by the classification of Lefevre *et al.*⁷ Angiographic restenosis was defined as diameter stenosis \geq 50% within a previously stented segment (stent and 5 mm proximal and distal) at the follow up angiogram. Focal restenosis was defined as a restenotic lesion \leq 10 mm long. Diffuse restenosis was defined as a restenotic lesion \geq 10 mm long.

Statistical analysis

Continuous variables are presented as mean (SD) or median with interquartile range and categorical variables are presented as frequencies with percentage. Data were statistically analysed with SPSS version 11.5 (SPSS Inc, Chicago, Illinois, USA). Continuous variables were compared by the independent sample t test or Mann-Whitney U test. Categorical variables were compared by the χ^2 statistic or Fisher's exact test. To identify factors that might have been related to angiographic restenosis, logistic regression models were used. The results are presented as odds ratios with 95% confidence intervals (CI). Survival free of TLR was estimated with the Kaplan-Meier method and the differences between curves were evaluated by the log rank test. The influence of baseline variables on the one year rate of TLR was evaluated with Cox proportional hazards regression analysis, with entry and stay criteria of < 0.20 and < 0.10, respectively. The following baseline clinical, angiographic, and procedural variables were entered into the multivariate models: diabetes, unstable angina, kissing balloon post-dilatation, baseline reference vessel diameter, lesion length, post-procedural minimum lumen diameter, and stent length. The results are presented as hazard ratios with 95% CI.

RESULTS

Baseline and procedural characteristics

We identified 182 consecutive patients (with 186 bifurcation lesions). Group C comprised 121 patients (80 patients treated with SES and 41 patients treated with PES) and group T comprised 61 patients (46 patients treated with SES and 15 patients treated with PES). The two groups did not differ significantly regarding baseline clinical characteristics (table 1).

Table 2 lists baseline lesion characteristics and table 3 lists procedural characteristics. Compared with group T, in group C mean stent length at the side branch was longer (24.8 (8.5) mm ν 19.8 (9.9) mm, p = 0.001). Kissing balloon post-dilatation tended to be used more often in group T (73.8% ν 58.4%, p = 0.05).

Quantitative angiographic analysis

Table 4 shows results of quantitative coronary angiography. The two groups did not differ significantly regarding baseline and post-procedural quantitative coronary angiography results in either the main branch or the side branch.

Angiographic follow up was available for 96 (79.3%) patients (with 99 bifurcation lesions) in group C and for 46 (75.4%) patients (with 46 bifurcation lesions) in group T (p = 0.57) at a median period of 8.5 months (interquartile range 6.2–10.1 months) after the index procedure in group C

	Entire cohort (n = 182)	Group C (n = 121)	Group T (n = 61)	p Value*
Age (years)	62 (11)	62 (11)	61 (11)	0.67
Men	161 (88.5%)	107 (88.4%)	54 (88.5%)	1.0
Current or former smoker	94 (51.6%)	65 (53.7%)	29 (47.5%)	0.44
Hypercholesterolaemia	126 (69.2%)	86 (71.1%)	40 (65.6%)	0.49
- Hypertension	116 (63.7%)	78 (64.5%)	38 (62.3%)	0.87
Diabetes mellitus	45 (24.7%)	29 (24.0%)	16 (26.2%)	0.86
Prior MI	74 (40.7%)	45 (37.2%)	29 (47.5%)	0.20
Prior CABG	33 (18.1%)	24 (19.8%)	9 (14.8%)	0.54
Unstable angina	36 (19.8%)	26 (21.5%)	10 (16.4%)	0.56
LVEF (%)	52.4 (8.5)	52.9 (8.6)	51.3 (8.3)	0.23
Glycoprotein IIb/IIIa inhibitors	83 (45.4%)	60 (49.6%)	23 (37.7%)	0.17

3

1

40

4b

Lesion location

LCX/OM

LAD/diagonal

Table 2 Baseline lesion characteristics						
	Entire cohort	Group C	Group T	p Value*		
Number of lesions	186	125	61			
Total occlusion						
Main branch	11 (5.9%)	7 (5.6%)	4 (6.6%)	0.75		
Side branch	8 (4.3%)	7 (5.6%)	1 (1.6%)	0.28		
Restenotic lesions	` '		, ,			
Main branch	28 (15.1%)	15 (12%)	13 (21.3%)	0.13		
Side branch	21 (11.3%	11 (8.8%)	10 (16.4%)	0.14		
Lesion type	•	, ,	, ,	0.78		
1 ''	128 (68.8%)	84 (67.2%)	44 (72.1%)			
2	21 (11.3%)	14 (11.2%)	7 (11.5%)			

19 (10.2%)

119 (64.0)

49 (26.3)

18 (9.7)

11 (5.9%)

5 (2.7%)

2 (1.1%)

RCA/RCA-PL/RCA-PD Values are number (%).

*Group C versus group T.

LAD, left anterior descending artery; LCX, left circumflex artery; OM, obtuse marginal; PD, posterior descending; PL, posterior lateral; RCA, right coronary artery

and 8.8 months (interquartile range 4.8-10.6 months) in group T (p = 0.94). The two groups did not differ significantly regarding the rate of restenosis (main branch: 16.2% of group C ν 13.0% of group T, p = 0.8; side branch: 19.2% of group C ν 26.1% of group T, p = 0.39). However, in the lesions treated with kissing balloon post-dilatation, the restenosis rate of the side branch was lower in group C than in group T (8.6% ν 26.5%, p = 0.04), with a lower late of lumen loss (0.23 (0.21) mm ν 0.37 (0.33) mm, p = 0.02). In the lesions in which kissing balloon post-dilatation was not performed, the late lumen loss of the side branch was higher in group C than in group T (0.71 (0.62) mm ν 0.44 (0.43) mm, p = 0.03) (fig 1).

With regard to the angiographic pattern of restenosis, the two groups did not differ significantly in either the main or the side branch. In group C, 19 restenotic lesions were limited to the side branch (restenosis was focal ostial in nine, diffuse in six, and totally occluded in four lesions). In group T, 13 restenotic lesions were found in the side branch, of which nine were focal ostial, three diffuse, and one totally occluded. In the main branch, 16 restenotic lesions were found in group C (focal in-stent restenosis in 12, diffuse in two, and totally occluded in two) and six were found in group T (focal instent restenosis in four and diffuse in two).

Clinical outcomes

8 (6.4%)

4 (3.2%)

2 (1.6%)

83 (66.4)

30 (24.0)

12 (9.6)

13 (10.4%)

3 (4.9%)

6 (9.8%)

1 (1.6%)

36 (59.0)

19 (31.1)

6 (9.8)

Table 5 shows in-hospital results and clinical follow up outcomes. Clinical follow up data at one year were available for all patients. Two cases of O wave AMI were documented in group C: one occurred in hospital due to occlusion of the septal branches during the index procedure; the other occurred at 3.6 months due to stent thrombosis, which developed in the left circumflex, and the bifurcation lesions (right coronary artery and acute marginal) treated in the index procedure were known to be occluded from a prior angiogram, with no adverse clinical events. During one year's follow up, one (0.8%) patient in group C died of heart failure (3.7 months after the procedure). Compared with group T, the rate of revascularisation, both TLR and TVR, were lower in group C (TLR: 14.0% v 31.1%, p = 0.01; TVR: 16.5% v 32.8%, p = 0.02). The rate of TLR-free survival at one year was 86.0% in group C and 68.9% in group T (p = 0.005) (fig 2).

0.78

Two (1.7%) patients had intraprocedural stent thrombosis (both patients treated with SES) in the group C; one of them developed a periprocedural non-Q wave AMI. No elective glycoprotein IIb/IIIa inhibitors were given to either patient. Their total stent lengths were 105 mm and 51 mm, respectively. After intraprocedural thrombolytic treatment and further balloon inflation, thrombosis resolved. Two cases of

	Entire cohort	Group C	Group T	p Value*
Number of lesions	186	125	61	
Adjunctive debulking				
Main branch	5 (2.7%)	4 (3.2%)	1 (1.6%)	1.0
Side branch	3 (1.6%)	1 (0.8%)	2 (3.3%)	0.25
Mean stent length (mm)	, ,	, ,	, ,	
Main branch	28.9 (11.5)	29.4 (10.9)	27.6 (12.6)	0.32
Side branch	23.2 (9.3)	24.8 (8.5)	19.8 (9.9)	0.001
Maximum inflation pressur	e (atm)	, ,	` '	
Main branch	15.6 (3.0)	15.8 (3.0)	15.0 (3.0)	0.10
Side branch	14.7 (2.8)	14.7 (2.7)	14.7 (2.9)	0.97
Maximum balloon diamete	er (mm)	, ,	` '	
Main branch	3.06 (0.38)	3.08 (0.39)	3.02 (0.34)	0.28
Side branch	2.69 (0.34)	2.71 (0.35)	2.66 (0.33)	0.40
Final kissing balloon	118 (63.4%)	73 (58.4%)	45 (73.8%)	0.05

	Group C			Group T		
	Baseline	Post-procedural	Follow up	Baseline	Post-procedural	Follow up
Number of lesions	125	125	99	61	61	46
Main branch						
Reference vessel diameter (mm)	2.74 (0.52)	3.26 (0.45)	3.08 (0.63)	2.78 (0.52)	3.21 (0.40)	3.14 (0.51)
Minimum lumen diameter (mm)	0.93 (0.51)	2.86 (0.44)	2.29 (0.89)	0.87 (0.44)	2.87 (0.44)	2.41 (0.79)
Diameter stenosis (%)	66.4 (16.8)	11.9 (7.7)	26.7 (22.5)	68.7 (15.2)	10.5 (7.9)	23.6 (20.9)
Lesion length (mm)	16.0 (9.8)	NA	7.8 (6.6)	16.3 (10.1)	NA	6.4 (5.0)
Late lumen loss (mm)	0.42 (0.39)	0.34 (0.35)				
Side branch						
Reference vessel diameter (mm)	2.34 (0.48)	2.85 (0.48)	2.64 (0.53)	2.40 (0.46)	2.79 (0.48)	2.71 (0.50)
Minimum lumen diameter (mm)	0.84 (0.48)	2.42 (0.44)	1.77 (0.93)	0.80 (0.37)	2.44 (0.42)	1.88 (0.75)
Diameter stenosis (%)	63.7 (18.9)	14.9 (9.2)	34.2 (30.0)	66.8 (13.7)	13.3 (9.7)	30.1 (26.0)
Lesion length (mm)	10.5 (6.9)	NA .	6.8 (4.6)	10.9 (7.9)	NA .	5.7 (4.2)
Late lumen loss (mm)	0.44 (0.38)	0.42 (0.37)				

post-procedural stent thrombosis were adjudicated in group C. One patient (treated with SES) had a non-Q wave AMI 10 days after premature discontinuation of dual antiplatelets for abdominal surgery (28 days after the index procedure) and had angiographic documentation of stent thrombosis; the other patient (treated with PES) died suddenly 4.5 months after the index procedure.

By logistic regression analysis, diabetes (odds ratio 2.23, 95% CI 1.15 to 4.35, p=0.02) and absence of kissing balloon post-dilatation (odds ratio 1.87, 95% CI 1.01 to 3.46, p=0.047) were identified as predictors of angiographic restenosis. Post-procedural minimum lumen diameter (per millimetre) was identified as the only predictor of TLR at one year (hazard ratio 0.46, 95% CI 0.24 to 0.87, p=0.02). Absence of kissing balloon post-dilatation was a weak predictor of TLR (hazard ratio 1.98, 95% CI 0.98 to 4.03, p=0.058).

DISCUSSION

Although we cannot make any statement regarding the most suitable technique to treat bifurcation lesions (provisional stenting or stenting both branches), whenever two stents are needed the following conclusions can be drawn from this study. Firstly, compared with historical controls in which two bare metal stents were used in bifurcation lesions, implantation of two DES is associated with a lower rate of restenosis and need for revascularisation at long term follow up. Secondly, a significantly lower rate of restenosis in the side branch was observed in lesions treated with crush stenting and kissing balloon post-dilatation than with the T stenting technique. Thirdly, compared with the T stenting technique, crush stenting reduced the need for revascularisation, either TLR or TVR. Lastly, the absence of kissing balloon inflation was identified as one of the predictive factors for restenosis.

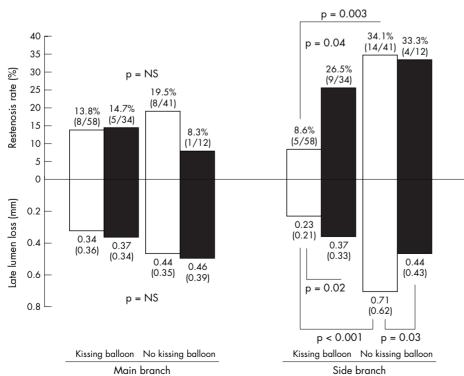


Figure 1 Restenosis rates of the crush (white bars) and T stenting (black bars) techniques with and without kissing balloon post-dilatation. Values are number (%) or mean (SD). NS, not significant.

	Entire cohort (n = 182)	Group C (n = 121)	Group T (n = 61)	p Value
In-hospital MACE	11 (6.0%)	9 (7.4%)	2 (3.3%)	0.34
Cardiac death	0	0	0	
AMI	11 (6.0%)	9 (7.4%)	2 (3.3%)	0.34
Q wave AMI	1 (0.5%)	1 (0.8%)	0	0.73
Non-Q wave AMI	10 (5.5%)	8 (6.6%)	2 (3.3%)	0.56
TLR	0	0	0	
TVR	0	0	0	
Cumulative one year MACE	54(29.7%)	32 (26.4%)	22 (36.1%)	0.23
Cardiac death	1 (0.5%)	1 (0.8%)	0	0.73
AMI	14 (7.7%)	12 (9.9%)	2 (3.3%)	0.20
Q wave AMI	2 (1.1%)	2 (1.7%)	0	0.80
Non-Q wave AMI	12 (6.6%)	10 (8.3%)	2 (3.3%)	0.34
TLR	36 (19.8%)	17 (14.0%)	19 (31.1%)	0.01
TVR	40 (22.0%)	20 (16.5%)	20 (32.8%)	0.02
Stent thrombosis				
Intraprocedural	2 (1.1%)	2 (1.7%)	0	0.80
Subacute	1 (0.5%)	1 (0.8%)	0	0.73
Late	1 (0.5%)	1 (0.8%)	0	0.73

AMI, acute myocardial infarction; MACE, major adverse cardiac events; TLR, target lesion revascularisation; TVR, target vessel revascularisation.

Value of kissing balloon post-dilatation in the crush stenting technique

The restenosis rate and TLR after implantation of two bare metal stents in bifurcation lesions were 40.6-62% and 37.5-38%, respectively.9-11 During the era of bare metal stents, the recommended strategy was implantation of one stent in the main branch with balloon dilatation of the side branch. Recently, several studies have shown the safety and efficacy of SES for the treatment of bifurcation lesions.1 12 13 However, these studies did not show the superiority of any strategy over the others. In addition, the SES bifurcation study showed that the restenosis rate in the side branch was as high as 21.8% after the implantation of two SES.1 Incomplete coverage of the side branch ostium may be related to the occurrence of restenosis at this site. The crush technique has been introduced to ensure optimal coverage of the ostium of the side branch.2 In our preliminary experience with DES implantation with the crush stenting technique, we did not observe a clear improvement in

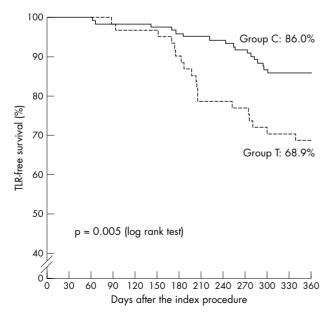


Figure 2 Kaplan-Meier survival curves for freedom from target lesion revascularisation (TLR) at one year's follow up. Group C, crush stenting; group T, T stenting.

the rate of restenosis at the ostium of the side branch. In the present study, the restenosis rate of the side branch treated with the crush stenting technique was not significantly reduced compared with treatment with the T stenting technique. However, if we analyse patients in whom kissing balloon post-dilatation was used, the restenosis rate in the side branch in group C was 8.6% and 26.5% in group T (p = 0.04). In our study, the absence of final kissing balloon use was identified as one of the predictors of restenosis. It is intriguing to note that late lumen loss was higher in the side branch after crush stenting without final kissing balloon dilatation than in the lesions treated with the T stenting technique (0.71 (0.62) mm v 0.44 (0.43) mm, p = 0.03). A possible explanation for these results is stent deformation or underexpansion with subsequent incomplete contact of the stent struts with the ostium of the side branch.¹⁴ On the basis of the results of this study, it is appropriate to state that when the crush stenting technique is used, high pressure side branch post-dilatation followed by kissing balloon post-dilatation are pivotal steps to reduce the rate of restenosis of the side branch.

It is worth noting that late lumen loss after the crush stenting technique is still relatively high, even with the use of kissing balloon post-dilatation. The reason for this finding remains unclear. To improve on these results further, specific stent designs addressing proper coverage of the ostium of the side branch may be needed. Some findings of this retrospective analysis, such as a possible advantage of crush with kissing versus the T technique, need to be confirmed in dedicated randomised studies.

Safety of the crush stenting technique

After the introduction of crush stenting, concerns were raised about this technique because of the theoretical risk of stent thrombosis secondary to a high metal density at the site of the carina. In the present study, two patients in the crush stenting group had intraprocedural stent thrombosis. It is must be pointed out that no elective glycoprotein IIb/IIIa inhibitors were given to either patient, which might have reduced the risk of intraprocedural thrombotic complications. In addition, the total stent length in these two cases was 105 mm and 51 mm, respectively. Recently, stent length was found to be associated with the occurrence of intraprocedural stent thrombosis. There were two cases of post-procedural stent thrombosis in group C. One patient developed subacute stent thrombosis after premature discontinuation of dual antiplatelet treatment. Owing to the small number of patients, the data in the present

study are insufficient to state whether the risk of stent thrombosis is higher after crush stenting technique. To reduce the risk of thrombotic events, a more liberal use of glycoprotein IIb/IIIa inhibitors should be considered.¹ ¹⁵ Furthermore, strict adherence to dual antiplatelet treatment is necessary.¹⁶

Limitations

The present study had some limitations. Firstly, it was a retrospective study with a small sample size. The choice of stenting strategy and the decision to use kissing balloon post-dilatation were at the operator's discretion and were non-randomised. Secondly, not all patients underwent angiographic follow up. Thirdly, we are not completely certain whether all the restenotic lesions located at the ostium of the side branch were functionally important; for some of them a severe angiographic stenosis may have been considered sufficient for a repeat intervention. Despite these limitations, the efficacy of kissing balloon post-dilatation in reducing the rate of side branch restenosis appears clear and the two groups were very similar in terms of baseline characteristics.

Conclusions

In non-selected bifurcation lesions treated with DES, the restenosis rate remains relatively high in the side branch. Compared with the T stenting technique, crush stenting with kissing balloon post-dilatation is associated with a low rate of restenosis in the side branch. Kissing balloon post-dilatation is mandatory when this technique is used.

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Committee on Publication Ethics – Seminar 2006

9.30am-5pm Friday 10th March 2006, BMA House, London, UK

This year's seminar takes an international perspective and addresses publication ethics and research in several European countries and beyond, with interactive workshops on common ethical and editorial dilemmas. The manipulation of impact factors, and whether unethical, will also be considered.

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- Professor Michael Farthing the Panel for Research Integrity (UK)
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